## (19) World Intellectual Property Organization

International Bureau



# 

#### (43) International Publication Date 8 April 2004 (08.04.2004)

#### PCT

### (10) International Publication Number WO 2004/029221 A3

(51) International Patent Classification7: A01N 1/02, C12M 1/00, 1/34, 3/00, C12N 5/00, 5/02, 5/06, 5/10

TRUSKEY, George [US/US]; 921 Monmouth Avenue, Durham, NC 27701 (US). KAPUR, Ravi [US/US]; 292 Morton Street, Stoughton, MA 02072 (US).

(21) International Application Number:

PCT/US2003/030965

(74) Agents: CLARK, Paul, T. et al.; Clark & Elbing LLP, 101 Federal Street, Boston, MA 02110 (US).

(22) International Filing Date:

29 September 2003 (29.09.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/414,065 27 September 2002 (27.09.2002) US 60/414,258 27 September 2002 (27.09.2002) US 60/414,102 27 September 2002 (27.09.2002) US

(63) Related by continuation (CON) or continuation-in-gart (CIP) to earlier applications:

US 60/414,065 (CIP) Filed on 27 September 2002 (27.09.2002) US 60/414,258 (CIP) Filed on 27 September 2002 (27.09.2002) US 60/414,102 (CIP) Filed on 27 September 2002 (27.09.2002)

(71) Applicants (for all designated States except US): THE **GENERAL HOSPITAL CORPORATION [US/US]; 55** Fruit Street, Boston, MA 02114 (US). GPB SCIENTIFIC LLC [US/US]; One Kendall Square, Cambridge, MA 02139 (US).

- (72) Inventors; and
- (75) Inventors/Applicants (for US only): TONER, Mehmet [TR/US]; 100 Pilgrim Road, Wellesley, MA 02481 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 13 May 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MICROFLUIDIC DEVICE FOR CELL SEPARATION AND USES THEREOF

(57) Abstract: The invention features methods for separating cells from a sample (e.g., separating fetal red blood cells from maternal blood). The method begins with the introduction of a sample including cells into one or more microfluidic channels. In one embodiment, the device includes at least two processing steps. For example, a mixture of cells is introduced into a microfluidic channel that selectively allows the passage of a desired type of cell, and the population of cells enriched in the desired type is then introduced into a second microfluidic channel that allows the passage of the desired cell to produce a population of cells further enriched in the desired type. The selection of cells is based on a property of the cells in the mixture, for example, size, shape, deformability, surface characteristics (e.g., cell surface receptors or antigens and membrane permeability), or intracellular properties (e.g., expression of a particular enzyme).



## INTERNATIONAL SEARCH REPORT

International application No.

		} ,	PC17US03/30965		
A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) : A01N 1/02; C12M 1/00, 1/34, 3/00; C12N 5/00, 5/02, 5/06, 5/10  US CL : 435/2, 283.1, 288.6, 325, 355  According to International Patent Classification (IPC) and back and in the International Patent Classification (IPC) and back and in the International Patent Classification (IPC) and back and in the IPC.					
According to International Patent Classification (IPC) or to both national classification and IPC  B. FIELDS SEARCHED					
Minimum doc	cumentation searched (classification system followed by 15/2, 283.1, 288.6, 325, 355	y classification symbols	)		
Documentatio None	on searched other than minimum documentation to the e	extent that such docume	ints are included in	the fields searched	
	ta base consulted during the international search (name ontinuation Sheet	of data base and, wher	e practicable, scar	ch terms used)	
C. DOCUMENTS CONSIDERED TO BE RELEVANT					
Category *	Citation of document, with indication, where ap			Relevant to claim No.	
Y,E	US 6,344,326 B1 (NELSON et al) 05 Fe bruary 2002, column 21, lines 40-52 and lines 55- 65, column 22, all lines and see abstract.				
Y	US 6,074,827 A (NELSON et al) 13 June 2000, columns 1-9, all lines and abstract. 1-67			1-67	
Y	US 6,432,630 B1 (BLANKENSTEIN) 13 August 2002, column 3, all lines and abstract.			1-67	
Y	US2002/0115201 A1 (BARENBURG et al) 22 August 2002, column 10, all lines and abstract.			1-67	
Y,E	US 6,632,619 B1 (HARRISON et al) 14 October 20003, columns 2-4, all lines and abstract.			1-67	
Y	US 6,613,525 B2 (NELSON et al) 02 September 2003, columns 27-28, all lines and abstract.			1-67	
Y	US 6,361,958 B1 (SHICH et al) 26 March 2002, columns 2-4, all lines and abstract.			1-67	
Y	US 6,007,690 A (NELSON) et al 28 December 1999, column 20, all lines, column 21, lines 1-15, and abstract.			1-67	
Y,p	US 6,529,835 B1 (WADA et al), columns 16-21 04 March 2003, all lines and abstract.			1-67	
Further	documents are listed in the continuation of Box C.	See patent fa	amily annex.		
"A" document	pecial categories of cited documents:  t defining the general state of the art which is not considered to be	date and not in	published after the inte conflict with the applic cory underlying the inve	rnational filing date or priority atlon but cited to understand the ention	
	plication or patent published on or after the international filing date	considered no	el or cannot be conside	claimed invention cannot be red to involve an inventive step	
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination			
	t referring to an oral disclosure, use, exhibition or other means	5	to a person skilled in th	e art	
"P" document published prior to the international filing date but later than the priority date claimed			nber of the same patent		
Date of the actual completion of the international search		Date of mailing of the international search report			
21 February 2004 (21.02.2004)		25 MAR	CUUS 1		
	ailing address of the ISA/US	Authorized officer	4.11	1. //	
Mail Stop PCT, Attn: ISA/US Commissioner for Patents		Deborah K. Ware	Mill	a Collen for	
Ale	D. Box 1450 xandria, Virginia 22313-1450 (2703) 305-3230	Telephone No. 703-3	08-0/96		
Facsimile No. (703) 305-3230					

	PCT/US03/30965		
INTERNATIONAL SEARCH DESCRIPTION	101/0003/00503		
INTERNATIONAL SEARCH REPORT	1		
Continuation of B. FIELDS SEARCHED Item 3:			
WEST; ANABSTR; CAPLUS; EMBASE; ESBIOBASE; IFIPAT; MEDLINI	E: PASCAL: PROMT: SCISEARCH USPATFULL:		
USPAT2	5, 1.100.15, 1.101.11, 00.111.101.101.11.101.11.101.11.1		
3321112			
}			
1			
ì			
{			

Form PCT/ISA/210 (second sheet) (July 1998)